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TITLE: Randomized, Double Blind, Placebo Controlled Trial of
Neuroprotective Effects of Epoetin alfa in Patients
Receiving Adjuvant Chemotherapy for Breast Cancer

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13. ABSTRACT (Maximum 200 Words) Cognitive deficits (e.g. problems with memory and concentration) are common during and after adjuvant breast cancer chemotherapy, but the pathophysiology of these phenomena is known. Cognitive impairment can, certainly, limit a patient's quality of life. The treatment of the cognitive dysfunction has not been investigated. ^[15O] water activation using Positron Emission Tomography (PET) scan yields patterns of blood flow to brain regions used in specific cognitive skills. Studies with erythropoietin (EPO) on rat and mouse brains suggest that it protects the brain from ischemia, concussive brain injury, and toxin exposure and enhances cognitive function. We hypothesize that ^[15O] water PET scan along with neuropsychological tests can evaluate the effectiveness of EPO as a treatment for cognitive dysfunction and identify the pathophysiology of cognitive dysfunction in patients receiving. Patients with early stage breast cancer who are candidates for adjuvant chemotherapy will undergo ^[15O] water PET scans at baseline to measure the difference in regional blood flow of the brain during working memory. Specific neuropsychological test will be done to study the attention, speeded processing, memory, and executive functions outside of the scanner. When the patients start treatment with AC they will be randomized into two groups. One group will receive weekly injections with EPO and the other group will receive placebo. PET scans and neuropsychological studies will be repeated in these two groups at the end of 4 cycles of AC. The trial opened to accrual in April 2003 and there are currently three patients enrolled.				
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Grant/Contract/MIPR No.: DAMD17-02-1-0621

Principal Investigator: Jame Abraham, MD

Institution: West Virginia University
Morgantown, West Virginia

Report Title: Randomized Double Blind, Placebo Controlled Trial of Neuroprotective Effects of Epoetin alfa (Procrit®) in Patients Receiving Adjuvant Chemotherapy for Breast Cancer

Report Type: Annual Summary Report

Award Mechanism: Idea and Career Development Award

Date of Report: October 2003

Reporting Period: October 1st 2002 to September 30th 2003

Introduction:

Adjuvant treatment with doxorubicin and cyclophosphamide (AC) clearly prolongs the overall survival in women with breast cancer. In U.S.A only, over 100, 000 women will receive adjuvant chemotherapy for breast cancer every year. Cognitive deficits (e.g. problems with memory and concentration) are common during and after adjuvant breast cancer chemotherapy, but the pathophysiology of these phenomena is unknown. More importantly, treatment of the cognitive dysfunction, which can limit the quality of life of survivors, has not been investigated.

We hypothesize that [¹⁵O] water PET scan along with neuropsychological tests can evaluate the effectiveness of EPO as a treatment for cognitive dysfunction and identify the pathophysiology of cognitive dysfunction in patients receiving.

The specific aims of the study are to: examine the efficacy of EPO as a treatment of cognitive impairment associated with adjuvant chemotherapy for breast cancer and to examine the neural changes associated with cognitive dysfunction in patients receiving adjuvant chemotherapy for breast cancer using [¹⁵O] water PET scans

The clinical trial has started accruing patients in April 2003.

Body:**Task 1. Study the baseline function**

- Three patients with early stage breast cancer receiving adjuvant chemotherapy have been enrolled into the study.
- Baseline cognitive function assessment, with neuropsychological measures have been completed by all patients.
- The baseline study of regional blood flow of the brain using [^{15}O] water Positron Emission Tomography (PET) during working memory has been completed by all patients.

Task 2. To study the cognitive function after 4 cycles of chemotherapy with or without erythropoietin (EPO)

- 3 patients have been randomized to the study
- All patients have completed the treatment with AC and study drug per protocol
- All patients have completed the PET scans and neuropsychological measures per protocol.

Task 3. Analysis of the data and wiring of the final report

- All data is maintained in a cumulative database. Task 3 will be completed after the patient accrual goal is attained.

Key Research Accomplishments:

- West Virginia University received initial IRB approval of the aforementioned project on February 5, 2002.
- The Department of Defense requested many changes to the protocol and the consent form at that time; it was resubmitted to the IRB as an amendment on August 20, 2002. Due to the nature and the quantity of changes requested by the sponsor, the IRB required the protocol to be resubmitted to the full board as a new protocol. Hence, the protocol was prepared and submitted to the IRB on September 20, 2002 and approved on October 21, 2002.
- The trial was again amended to remove Ortho Biotech as a sponsor, in addition, to other minor changes. The amended protocol and consent form was submitted to the IRB on December 9, 2002 and approved on December 31, 2002.
- The study became open to enrollment in April 2003.
- All patients seen in the comprehensive breast cancer program are screened for eligibility; the first patient was screened on April 14, 2003. The first patient was enrolled into the study on April 28, 2003 and the second patient was enrolled on May 29, 2003.
- The patients on study are treated and followed per study criteria.
- There have been no reports of serious adverse events.

Reportable Outcomes:Research article

Abraham, J, et al., **Cognitive Impairment in Patients Treated with Adjuvant Systemic Therapy for Breast Cancer: Role of Positron Emission Tomography (PET) Scan and Erythropoietin**, *Oncologist*, submitted for publication 2003.

Presentation

Invited Speaker, "Use of PET Scanning in Assessing the Pathophysiology of Cognitive Dysfunction: The Future of Supportive Therapy in Oncology an International Congress," Hamilton, Bermuda, March 13, 2003.

Conclusions:

The study is in the earliest phase. Accrual was initiated in April 2003. The data will be analyzed when the study accrual is completed.